



INDIANA HEALTH COVERAGE PROGRAMS

PROVIDER REFERENCE MODULE

Genetic Testing

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Revision History

Version	Date	Reason for Revisions	Completed By
1.0	Policies and procedures as of October 1, 2015 Published: February 25, 2016	New document	FSSA and HPE
1.1	Policies and procedures as of April 1, 2016 Published: October 18, 2016	Scheduled update	FSSA and HPE
2.0	Policies and procedures as of May 1, 2017 Published: August 15, 2017	Scheduled update	FSSA and DXC
3.0	Policies and procedures as of June 1, 2018 Published: October 16, 2018	Scheduled update: <ul style="list-style-type: none"> • Reorganized and edited text for clarity • Updated the note box at the beginning of module to reflect new standard wording • Incorporated information from relevant sections of the <i>Medical Policy Manual</i> and removed references to that document • Removed all code table references because the corresponding code document, <i>Genetic Testing Codes</i>, was removed from the website • Added genetic testing definition and information about the genetic counselor provider specialty in the Introduction section • Updated the Chromosomal Microarray Analysis section, including adding coverage criteria and definitions, and removing billing guidelines • Updated the Human Epidermal Growth Factor Receptor 2 (HER-2/neu) Gene Detection Test and HER2 Protein Overexpression Test section • Updated the BRCA1 and BRCA2 Genetic Testing for Breast, Ovarian, and Related Cancers section, including adding coverage criteria 	FSSA and DXC

Version	Date	Reason for Revisions	Completed By
		<ul style="list-style-type: none">Updated the <i>Gene Expression Profiling for the Management of Breast Cancer – Oncotype DX Breast Recurrence Score Testing</i> section, including adding coverage criteria and removing the list of noncovered tests	

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Note: For updates to coding, coverage, and benefit information, see the [IHCP Banner Pages and Bulletins](#) at indianamedicaid.com.

The information in this module applies to services provided under the fee-for-service delivery system. Within the managed care delivery system, individual managed care entities (MCEs) establish their own coverage criteria, prior authorization requirements, billing procedures, and reimbursement methodologies. For services covered under the managed care delivery system, providers must contact the Healthy Indiana Plan (HIP), Hoosier Care Connect, or Hoosier Healthwise member's MCE or refer to the MCE provider manual for specific policies and procedures. MCE contact information is included in the [IHCP Quick Reference Guide](#) available at indianamedicaid.com.

Introduction

According to the National Human Genome Research Institute, the term *genetic testing* covers an array of techniques, including analysis of human DNA, RNA, or protein. In the clinical setting, genetic tests can be performed to do the following:

- Confirm a suspected diagnosis.
- Predict the possibility of future illness.
- Detect the presence of a carrier state in unaffected individuals whose children may be at risk.
- Predict response to therapy.

Genetic tests are also performed to screen fetuses, newborns, or embryos used in in-vitro fertilization for genetic defects.

Effective November 1, 2017, professionally licensed genetic counselors can enroll as Indiana Health Coverage Programs (IHCP) providers. These providers are enrolled as provider type 36 – *Genetic Counselor* with specialty 800 – *Genetic Counselor*. See the [Provider Enrollment](#) module for more information.

Prior Authorization for Genetic Testing

Prior authorization (PA) is required for all genetic testing, unless otherwise noted within the [Professional Fee Schedule](#) at indianamedicaid.com or by a test-specific coverage policy.

PAs are test-specific, and providers must follow all available guidelines established by the American College of Medical Genetics. If no guidelines are available, providers should follow commonly accepted medical guidelines, such as Amsterdam II or revised Bethesda guidelines for hereditary nonpolyposis colorectal cancer (HNPCC) diagnoses. All IHCP policy guidelines must also be met for PA approval.

The following documentation is required for PA review:

- Documentation outlining medical necessity, specifically stating the impact on the patient's treatment
- Documentation that genetic counseling has been performed prior to testing
- Results from any commonly used conventional diagnostic testing showing inconclusive diagnosis
- All other general documentation required for PA

For more information about PA requests, see the [Prior Authorization](#) module.

Coverage Criteria for Genetic Testing

The IHCP covers a variety of genetic tests when provided in compliance with IHCP coverage and billing guidelines, including obtaining PA when required. IHCP coverage of these services is subject to limitations established for certain benefit plans and in accordance with the policies and procedures described in this module.

Genetic testing services are **not** covered under the following circumstances:

- For the sole convenience of information for the patient without impacting treatment
- For the medical management of other family members, unless otherwise specified in policy
- For the establishment of paternity
- All screening tests, except the screening tests listed under the State's required newborn screening policy (see *Indiana Administrative Code 410 IAC 3-3-3* and the [Inpatient Hospital Services](#) module)
- If history, physical examination, pedigree analysis, genetic counseling, or completion of conventional diagnostic studies has given a definitive diagnosis
- If a genetic test has previously been performed to provide a conclusive diagnosis of the same genetic disorder

Reimbursement for genetic tests specific to a gene or a condition is limited to once per member per lifetime, unless otherwise specified in a test-specific coverage policy. For genetic tests *not* specific to a gene or a condition, providers must have medical documentation on file indicating that each testing procedure is for a separate and distinct diagnosis. The IHCP does not cover genetic testing panels unless otherwise stated.

All the following general criteria must be met for any genetic testing service to be covered:

- The genetic disorder must be associated with a potentially significant disability.
- The risk of the significant disability from the genetic disorder cannot be identified through biochemical or other testing (for example, ultrasound screening for aortic disease in Marfan's syndrome).
- A specific mutation, or set of mutations, has been established in scientific literature to be reliably associated with the disease.
- The results of the genetic test could impact the medical management of the member with improved net-health outcomes.
- No determinable diagnosis can be gathered from the history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies.
- Prior authorization is obtained, if required.

In addition to these general criteria, test-specific guidelines established by the American College of Medical Genetics must also be met. This module outlines guidelines for the following categories of genetic tests: molecular pathology, cytogenetics, and multianalyte assays with algorithmic analyses (MAAA).

Molecular Pathology

Molecular pathology procedures are medical laboratory procedures involving analyses of nucleic acid to detect variants in genes that may be indicative of germline conditions (for example, constitutional disorders) or somatic conditions (for example, neoplasia), or to test for histocompatibility antigens (such as the human leukocyte antigen [HLA]).

The IHCP covers many molecular pathology tests.

Cytogenetics

The National Human Genome Research Institute defines *cytogenetics* as the branch of genetics that studies the structure of DNA within the cell nucleus. Cytogenetics studies the number and morphology of chromosomes, using chromosome banding techniques (classical cytogenetics) or hybridization fluorescently labeled probes (molecular cytogenetics).

Most cytogenetic tests are IHCP-covered services.

Multianalyte Assays with Algorithmic Analyses

MAAAs are procedures that use multiple results derived from assays of various types, including molecular pathology assays, fluorescent in situ hybridization assays, and non-nucleic-acid-based assays (such as proteins, polypeptides, lipids, and carbohydrates). Algorithmic analysis using the results of these assays as well as other patient information is then performed and reported, typically as a numeric score or a probability.

MAAA procedures are not covered by the IHCP unless specifically stated, because they do not provide a definitive diagnosis or change the course of treatment.

Additional Information for Specific Types of Genetic Testing

The following sections include additional coverage guidelines for certain types of genetic testing.

Chromosomal Microarray Analysis

The IHCP covers chromosomal microarray analysis (CMA) testing when it is determined to be medically necessary for diagnosing a genetic abnormality in children with apparent nonsyndromic cognitive developmental delay/intellectual delay (DD/ID) or autism spectrum disorder (ASD), according to the latest accepted *Diagnostic and Statistical Manual of Mental Disorders* (DSM) guidelines.

CMA testing is **not** considered medically necessary and will **not** be covered under the following circumstances:

- To confirm the diagnosis of a disorder or syndrome that is routinely diagnosed based on clinical evaluation alone
- For prenatal genetic testing
- For the screening, diagnosis, and management of hematologic or oncologic malignancies
- As a means to predict or evaluate pregnancy loss
- In cases of family history of chromosome rearrangement in a phenotypically normal individual
- In all other cases of suspected genetic abnormality in children with DD/ID or ASD

Prior authorization for CMA testing requires documentation of **all** the following:

- Any indicated biochemical tests for metabolic disease have been performed, and results are nondiagnostic.
- FMR1 gene analysis (for Fragile X), when clinically indicated, is negative.
- In addition to a diagnosis of nonsyndromic DD/ID or ASD, the child has one or more of the following:
 - Two or more major malformations
 - A single major malformation or multiple minor malformations in an infant or child who is also small-for-dates
 - A single major malformation and multiple minor malformations
- The results for the genetic testing have the potential to impact the clinical management of the patient.
- Testing is requested after the parent(s) have been engaged in face-to-face genetic counseling with a healthcare professional who is licensed under *Indiana Code IC 25-17.3*.

Note: The following definitions are from the American College of Medical Genetics Guidelines, Evaluation of the Newborn with Single or Multiple Congenital Abnormalities:

- A **malformation** refers to abnormal structural development.
 - A **major malformation** is a structural defect that has a significant effect on function or social acceptability, such as ventricular septal defect or cleft lip.
 - A **minor malformation** is a structural abnormality that has a minimal effect on function or social acceptance, such as preauricular ear pit or partial syndactyly (fusion) of the second or third toes.
- A **syndrome** is a recognizable pattern of multiple malformations. Syndrome diagnoses are often relatively straightforward and common enough to be clinically recognized without specialized testing. Examples include Down syndrome, neural tube defects, and achondroplasia. However, in the very young, or in the case of symptoms with variable presentation, confident identification may be difficult without additional testing.

Genetic Testing for Cancer Susceptibility

Several genetic tests exist for a determination of risk (or risk score) associated with inheritable cancer susceptibility, such as for breast and ovarian cancer or hereditary nonpolyposis colorectal cancer (HNPCC). Providers should check the [Fee Schedules](#) at indianamedicaid.com for coverage of specific tests.

Cancer-susceptibility genetic testing is a covered service when the general criteria **and both** the following conditions are met:

- A specific mutation, or set of mutations, has been established in the scientific literature to be reliably associated with the risk of developing malignancy.
- The results of the genetic test potentially affect at least one of the management options considered by the physician, in accordance with accepted standards of medical care, including any one of the following:
 - Surgery, or the extent of surgery
 - A change in surveillance
 - Hormonal manipulation
 - A change in standard therapeutic or adjuvant chemotherapy

All criteria set forth in test-specific coverage policies must also be met.

Human Epidermal Growth Factor Receptor 2 (HER2/neu) Gene Detection Test and HER2 Protein Overexpression Test

The IHCP covers laboratory testing for HER2 protein overexpression and HER2/neu gene detection when medically necessary for members who have been diagnosed with a malignant neoplasm of the breast. Prior authorization is not required for HER2 testing. However, documentation of medical necessity is required. The ordering physician must have documentation in the member's medical records to support the medical necessity of the tests ordered.

BRCA1 and BRCA2 Genetic Testing for Breast, Ovarian, and Related Cancers

The IHCP covers BRCA1 and BRCA2 testing when it is determined to be medically necessary based on personal history or family history, as described in this section. Prior authorization is required.

IHCP members referred to an oncologist or geneticist for BRCA1 and BRCA2 testing must have a completed personal and family cancer history that should include three generations on both maternal and paternal sides of the family in the member's medical record to include the following:

- Relatives with breast, ovarian, and other relevant cancers, such as prostate and colon cancer
- Age at diagnosis in affected family members
- Other significant factors, such as ethnic background

Providers must submit documentation with the PA request and must maintain the documentation in the member's medical record.

BRCA1 and BRCA2 genetic testing is considered medically necessary for members with a **personal history** of at least one of the following:

- Breast cancer diagnosis at age 45 or younger, with or without family history
OR
Breast cancer diagnosis at age 50 or younger and one or more of the following:
 - Two breast primary cancers, with the first breast cancer diagnosis occurring at age 50 or younger
 - At least one close blood relative with breast cancer at age 50 or younger
 - At least one close blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer diagnosed at any age
 - A limited family history or adopted
- Diagnosed at age 60 or younger with triple-negative (ER-, PR-, HER2-) breast cancer
- Breast cancer diagnosed at any age and one or more of the following:
 - Two breast primary cancers in a single individual with at least one close blood relative with breast cancer diagnosed at age 50 or younger
 - Two breast primary cancers in a single individual with at least one close blood relative with epithelial ovarian/fallopian tube/primary peritoneal cancer diagnosed at any age
 - Two or more close blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer diagnosed at any age
 - Two or more close blood relatives with pancreatic cancer diagnosed at any age
 - Two or more close blood relatives with prostate cancer (Gleason score of 7 or greater) diagnosed at any age
 - Close male blood relative with breast cancer (first-degree or second-degree blood relative allowable)
 - A close relative with a known BRCA1 or BRCA2 gene mutation
 - At least two close blood relatives on the same side of the family with other hereditary breast and ovarian cancer (HBOC)-syndrome-associated malignancies (prostate, pancreatic, melanoma)
 - Ethnicity associated with deleterious mutations, including Ashkenazi Jewish, Icelandic, Hungarian, Swedish, and Dutch
- Pancreatic, prostate (Gleason score of 7 or greater), or epithelial ovarian/fallopian tube/primary peritoneal cancer and two or more close blood relatives with at least one of the following:
 - Breast cancer diagnosed at any age
 - Ovarian cancer diagnosed at any age
 - Pancreatic cancer diagnosed at any age
 - Prostate cancer (Gleason score of 7 or greater) diagnosed at any age
- Male breast cancer diagnosis

BRCA1 and BRCA2 genetic testing is considered medically necessary for members with a **family history** of at least one of the following (no personal history required):

- Member has a relative with known BRCA1 or BRCA2 mutation
- Member has a male relative with breast cancer
- Female member of Ashkenazi Jewish, Icelandic, Hungarian, Swedish, or Dutch ancestry has one or more of the following:
 - One or more first-degree relative with breast cancer or epithelial ovarian cancer
 - Two or more second-degree relative on same side of family with breast cancer
 - Two or more second-degree relative on same side of family with epithelial ovarian cancer

- Female member not of Ashkenazi Jewish, Icelandic, Hungarian, Swedish, or Dutch ancestry has one or more of the following:
 - First-degree or second-degree relative with breast cancer and one or more of the following:
 - Diagnosed at age 45 or younger
 - Diagnosed at age 50 or younger with unknown or limited family history
 - Diagnosed at age 50 or younger with one or more close blood relatives with breast cancer diagnosed at any age
 - Diagnosed at age 60 or younger with triple-negative breast cancer
 - First-degree or second-degree relative with two breast primary cancers with the first primary diagnosed at age 50 or younger
 - First-degree or second-degree relative with breast cancer diagnosed at any age, who in turn has one or more of the following:
 - One or more close blood relatives with breast cancer diagnosed at age 50 or younger
 - One or more close male blood relatives with breast cancer diagnosed at any age
 - One or more close blood relatives with epithelial ovarian cancer diagnosed at any age
 - Two or more close blood relatives with breast cancer diagnosed at any age
 - Two or more close blood relative with pancreatic cancer diagnosed at any age
 - Two or more close blood relative with prostate cancer (Gleason score of 7 or greater) diagnosed at any age
 - First-degree or second-degree relative with breast cancer diagnosed at any age who is of male gender
 - First-degree or second-degree relative with breast cancer who is of ethnicity associated with deleterious mutations, including Ashkenazi Jewish, Icelandic, Hungarian, Swedish, or Dutch
 - First degree or second-degree relative with epithelial ovarian cancer diagnosed at any age
 - First-degree or second-degree relative with pancreatic cancer diagnosed at any age who in turn has two or more close blood relative with one or more of the following:
 - Breast cancer diagnosed at any age
 - Ovarian cancer diagnosed at any age
 - Pancreatic cancer diagnosed at any age
 - Prostate cancer (Gleason score of 7 or greater) diagnosed at any age
 - First-degree or second-degree relative with prostate cancer (Gleason score of 7 or greater) diagnosed at any age, who in turn has two or more close blood relatives with one or more of the following:
 - Breast cancer diagnosed at any age
 - Ovarian cancer diagnosed at any age
 - Pancreatic cancer diagnosed at any age
 - Prostate cancer (Gleason score of 7 or greater) diagnosed at any age
 - Third-degree relative with breast or epithelial ovarian cancer, who in turn has one or more of the following:
 - One close blood relative with epithelial ovarian cancer and another close blood relative with breast cancer diagnosed at age 50 or younger
 - Two or more close blood relatives with breast cancer with at least one diagnosed at age 50 or younger
 - Two or more close blood relatives with epithelial ovarian cancer diagnosed at any age

Definitions

For the purpose of this policy, the following definitions apply:

- Close blood relatives are first, second, and third degree relatives as defined below:
 - First-degree relatives include parents, siblings, and offspring
 - Second-degree relatives include half-brothers/-sisters, aunts/uncles, grandparents, grandchildren, and nieces/nephews affected on the same side of the family
 - Third-degree relatives include first cousins, great-aunt/-uncles, great-grandchildren, and great grandparents affected on the same side of the family
- A breast cancer diagnosis includes either invasive or non-invasive (ductal carcinoma in situ) types.
- Ovarian cancer also includes fallopian tube cancers and primary peritoneal carcinoma.
- Persons are not considered to have a limited family history unless they have fewer than two first-degree or second-degree female relatives or female relatives surviving beyond 45 years of age on either side of the family.
- Two breast primary cancers include cancers appearing at the same time (synchronous) and one is not a metastasis of the other, or primary cancers developing at intervals (metachronous). The tumors may be in one or two breasts.
- Hereditary breast ovarian cancer (HBOC)-syndrome -associated malignancies include prostate cancer, pancreatic cancer, or melanoma. The presence of these malignancies does not necessarily justify BRCA testing. For example, a female with breast cancer over age 50 whose sister had melanoma at 40 and whose father has prostate cancer would meet criteria. In another example a female with breast cancer over age 50 whose maternal aunt had pancreatic cancer and whose paternal uncle had prostate cancer would not meet criteria because the aunt and uncle are on different sides of the family.
- Triple-negative breast cancer refers to any breast cancer that does not express the genes for estrogen receptor (ER), progesterone receptor (PR), or HER2/neu. This subtype of breast cancer is clinically characterized as more aggressive and less responsive to standard treatment and is associated with poorer overall patient prognosis. It is diagnosed more frequently in younger women, women with BRCA1 mutations, and those belonging to African-American and Hispanic ethnic groups.

Billing and Reimbursement

BRCA1 and BRCA2 genetic testing is billed using the appropriate CPT^{®1} codes. The IHCP reimburses the manually priced genetic testing codes at 90% of billed charges.

Consistent with coding guidelines, the IHCP provides reimbursement once per member per lifetime for only one of the CPT procedure codes in the following code pairs:

- 81211 or 81214
- 81211 or 81216
- 81211 or 81162
- 81162 or 81214
- 81162 or 81216

If both codes in the code pair are billed, one of the codes will be denied with an explanation of benefits (EOB) 6276 – *Breast cancer analysis (BRCA1 & BRCA2) is not payable when a breast cancer analysis code has already been paid.*

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Additionally, if the IHCP has provided reimbursement for CPT code 81162, 81211, 81214, or 81216, the IHCP will not reimburse 81212, 81213, 81215, or 81217 for that member, because 81162, 81211, 81214, and 81216 represent *complete* BRCA1 and/or BRCA2 gene sequence analysis.

Gene Expression Profiling for the Management of Breast Cancer – Oncotype DX Breast Recurrence Score

The IHCP covers Oncotype DX Breast Recurrence Score when it is considered medically necessary for managing the treatment of breast cancer. Prior authorization is required. The 21-gene RT-PCR assay should only be ordered after surgery and subsequent pathological examination of the tumor have been completed. The test should be ordered in the context of a provider-patient discussion regarding risk preferences when the test result will aid in making decisions regarding chemotherapy.

Oncotype DX Breast Recurrence Score testing is billed using procedure code 81519 – *Test for detecting genes associated with breast cancer.*

To obtain PA for this test, all the following criteria must be met:

- Individual has had surgery, and a full pathological evaluation of the specimen has been completed.
- Histology is ductal, lobular, mixed, or metaplastic.
- Histology is not tubular or colloid.
- Estrogen receptor is positive (ER+), or progesterone receptor is positive (PR+), or both.
- HER2 receptor is negative.
- pN0 (node negative) or pN1mi with axillary lymph node micrometastasis is less than or equal to 2mm.
- Individual has one of the following:
 - Tumor size 0.6–1.0 cm moderate/poorly differentiated
 - Tumor size 0.6–1.0 cm well-differentiated with any of the following unfavorable features: angiolymphatic invasion, or high nuclear grade, or high histologic grade
 - Tumor size greater than 1.0 cm and less than or equal to 4.0 cm
- Individual does not have a pT4 lesion.
- Chemotherapy is a therapeutic option being considered and will be supervised by the practitioner ordering the gene expression profile.

Gene expression profiling with the Oncotype DX Breast Recurrence Score as a technique of managing the treatment of breast cancer is considered not medically necessary when the criteria listed have not been met.

Noncovered Services

Gene expression profiling as a technique of managing the treatment of breast cancer is considered **investigational and not medically necessary** when a gene profiling test *other than* the Oncotype DX Breast Recurrence Score is being used.

Gene expression profiling as a technique of managing the treatment of ductal carcinoma in situ (DCIS) is considered **investigational and not medically necessary** under all circumstances.

Repeat gene expression profiling with the Oncotype DX Breast Recurrence Score for the same tumor, such as a metastatic focus, or from more than one site when the primary tumor is multifocal, is considered **investigational and not medically necessary**.